Q & A

Oliver Hobert

Oliver Hobert is an Associate Professor at Columbia University Medical School in the Department of Biochemistry and Molecular Biophysics and is an Investigator with the Howard Hughes Medical Institute. He has obtained his Diploma degree in Biochemistry with Gerhard Krauss at the University of Bayreuth in Germany, and his PhD with Axel Ullrich at the Max Planck Institute for Biochemistry in Martinsried. He started to work on the nematode Caenorhabditis elegans *as a postdoc with Gary Ruvkun at MGH and Harvard Medical School. His laboratory investigates various aspects of nervous system development and function in* C. elegans*.*

What drew you into research on* C. elegans*? Mapping and cloning genes in *C. elegans* really took off in the late 80s, early 90s, with new interesting genes implicated in exciting biological processes popping up on a regular basis — and the ability to tightly link gene function to very specific biological processes really fascinated me when I started to look for a postdoc. I was very impressed with the depth in which cell lineage, fate, morphology, function, and so forth were described and catalogued in worms — which obviously provides a perfect starting point to define gene function in a physiologically relevant context through mutant analysis.

Another thing that really drew me to worms is the ability to have a pretty good overview over the whole organism. In spite of being a complex little critter, it is nevertheless simple enough that one can keep abreast of what's happening in each little subfield. One doesn't just become a this-or-that expert, knowing everything about one's favorite cell type or organ and nothing beyond that. That has allowed me in the past to get diverted into studying very different cell types, genes and cellular processes in the worm, which I really enjoy. From a developmental biology angle, this compactness also provides the wonderful and highly motivating perspective that the problem of how this organism with all its cell types develops from a fertilized egg will be solved some day.

If you had to choose again now, would you still go into* C. elegans*? Absolutely. In fact, my appreciation of the organism has deepened over time. As one harvests the fruits of genetic screens by mapping and cloning more and more genes involved in a given process, one really appreciates the conceptual beauty of forward genetics. Meaning that one can not only study the phenotypic consequences of the loss of a single gene in great detail, but take the next step and map out genetic pathways and genetic networks.

It is this extensive genetic analysis of specific processes that will remain in the domain of simple model systems for quite a while to come. Moreover, as the case of microRNAs most beautifully illustrates, phenotype-driven screens have and will continue to reveal the existence of unanticipated genetic processes. The fun is that one really never knows what one ends up with.

What are the most significant contributions that* C. elegans *research has provided so far? It would be sad if they could all be listed in a few sentences. Let me just mention one of the most recent ones, the identification of RNA-based gene regulation. The phenomenon of RNA interference (RNAi) was systematically dissected first in worms, by Andy Fire and Craig Mello, and it is probably fair to say that, all biology aside, RNAi is second only to PCR in terms of the storm with which a technique has taken over biological research. The credit of allowing the revelation of other RNA-based regulatory mechanisms, those mediated by microRNAs, lies even more clearly in the domain of worms. The key milestones here being Victor Ambros's fantastic detective work to figure out the molecular nature of the *lin-4* miRNA and Gary Ruvkun's ingeniously simple zoo blot that revealed the phylogenetic conservation of miRNAs that then really opened up the field. What's so important about the worm-based identification of RNA-mediated gene regulation is that it revealed the existence of a parallel universe out there, a new uncharted world. And what more could a researcher, basically a modern-day explorer, hope for?

Where do you see your research going in the next few years? My lab is rather diverse in its interests, but being so fascinated by the depth with which one can genetically dissect developmental pathways, a good part of my lab has focused on forward and reverse genetic approaches to understand the diversification of neuronal cell fates. The fate decision that we deal with most intensively is implemented across a rather mysterious axis, the left-right axis, which I find a fascinating problem. And luckily this fate decision, like many others, I believe, relies heavily on the use of the RNA inhabitants of the parallel universe mentioned above.

But whoever does the job, the long-term goal is to be able to trace back these cell specification decisions deep into the embryo, ultimately understanding the complete regulatory pathways that lead from a fertilized oocyte to a specific differentiated cell type, say a neuron in the nervous system. Doggedly determined application of good old classic genetics will lead us toward this goal. Or should this be called 'genet-omics' just to sound more trendy?

What was your first memorable encounter with science? Doing my first independent lab research project as an undergrad in 1990 with Alberto Mancinelli

at Columbia University, and sitting with him for hours in the dark room harvesting plants for measuring light responses and discussing World Cup soccer and pro tennis.

What are your views on scientific journals and publishing? When it comes to scientific journals, I am essentially a romantic. I love old, venerable society journals such as Genetics or other classics, they somehow breathe history and transcend the fashions of our times. I also happen to be naively optimistic about the maxim that quality will always win. Meaning, a good paper will be recognized as such no matter whether it was published in a flashy first-tier journal or in what is euphemistically called a 'more specialized journal'. At the end of the day, the important thing is the satisfaction that comes from having produced a unit of knowledge.

Do you have a favorite paper? Yes: the 1976 paper by John White and colleagues 'The structure of the ventral nerve cord of *Caenorhabditis elegans*' (Phil. Trans. R. Soc. Lond. B *275*, 327–348.), collectively referred to as 'The Mind of the Worm'. I pick this because the determined and painstaking effort that it took to map out the nervous system and the vast scope of a project like this provides such a beautiful illustration of how human's exploratory drive has shifted from the macroscopic mapping of our outer world, meaning the voyages of the old explorers, to the mapping of the microscopic universe, the inner world of other organisms and eventually ourselves.

Your advice to a young scientist? To always keep an open mind.

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Lethal munchies

The unpredictable but dramatic mass migration of Mormon crickets in the western US has been revealed to have a macabre twist. The insects are on the move as a result of food shortages and new research suggests that some insects find their fellow marchers the perfect snack: there's cannibalism in the pack.

Mormon crickets — *Anabrus simplex* — are large flightless grasshopper-like insects and not true crickets. Millions of them sometimes march together, with dozens of insects per square metre moving up to two kilometres a day, and covering an area up to 10 kilometres long. Marching troops of the omnivorous insects can cause serious crop damage, but unlike locusts they do not devour all the plants they encounter.

Curious to see if nutrition could explain this behaviour, Stephen Simpson at the University of Sydney, studied the crickets with Greg Sword at the US Department of Agriculture's research service, and colleagues Patrick Lorch and Iain Couzin, reporting in the Proceedings of the National Academy of Sciences (published online). They placed samples of foods rich in proteins or carbohydrates on a cattle trail in the path of the marching insects.

The crickets showed a clear preference for a protein-containing food, with up to 13 crickets clambering over a four-centimetre-wide dish at once. They also went after salt.

Foraging crickets prefer protein-rich sources such as seeds, flower heads and carrion. But there is not enough to go around. They get a lot from eating each other, says Simpson. "Mormon crickets are walking packages of protein and salt," he says. Any with reduced mobility are at increased risk of another cricket stopping to eat them.

Indeed, the researchers found cannibalism to be common. When checking to see the stomach contents of marching crickets the researchers found a substantial number contained the remains of other crickets.

The crickets do not swarm every year, only when there is not enough food to go round. They evidently tolerate cannibalistic companions because of the even greater risks of going alone: one study suggests that within two days more than half of isolated insects were eaten by other animals.

Salt march: A Mormon cricket on the move seeks protein and salt and will cannibalise other individuals to find it. (Photo: copyright Darin Oswald.)